REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 87 and 88 were previously pending in this application. Claim 1 is amended herein without prejudice or disclaimer. As a result, claims 1, 2, 87 and 88 are still pending for examination with claim 1 being an independent claim. No new matter has been added.

Rejection Under 35 U.S.C. § 112

Claims 1, 2, 87 and 88 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Applicant respectfully disagrees for the following reasons.

It is noted that the Examiner indicated that the claims were enabled for "administering an unmethylated CpG nucleic acid wherein the CpG nucleic acid *is an adjuvant nucleic acid* administered *in the presence of a vaccine* to a subject infected with an immune deficiency associated with HIV to induce an immune response to the vaccine and wherein the method does not treat HIV" (Office Action page 2; Emphasis added). The Examiner also stated on page 5 of the Office Action that "the instant claims recite use of CpG as an adjuvant." This is incorrect. Claim 1 as currently amended is reproduced below:

> A method for boosting a subject's immune system, the method comprising:
> administering an unmethylated CpG nucleic acid to a subject having an immune system deficiency associated with human immunodeficiency virus (HIV) infection in an effective amount to boost the subject's immune system.

Thus, the independent claim does <u>not</u> recite the use of CpG as an adjuvant. Applicant asserts that the instant invention is not limited to the use of a CpG as a vaccine adjuvant as interpreted by the Examiner. Rather, the claimed invention pertains to using immunostimulatory CpG oligonucleotides to boost the immune system of a subject having an immune system deficiency that is associated with an HIV infection. Thus the claimed invention embraces administering an

immunostimulatory CpG oligonucleotide either in the absence or in the presence of a vaccine. The claimed invention is not limited to the use of a CpG oligonucleotide as an adjuvant, *per se*. As described in the specification, an immunostimulatory CpG oligonucleotide, *administered alone*, can elicit immunostimulatory activity, without having a co-administered antigen. The CpG oligonucleotide can also be used as an adjuvant, for example, in conjunction with a vaccine, as noted by the Examiner. Applicant wishes to direct the Examiner's attention to page 31 of the specification as filed. The relevant passage is shown below:

> Based on their immunostimulatory properties, oligonucleotides containing at least one unmethylated CpG dinucleotide can be administered to a subject in vivo to treat an "immune system deficiency". Alternatively, oligonucleotides containing at least one unmethylated CpG dinucleotide can be contacted with lymphocytes (e.g. B cells or NK cells) obtained from a subject having an immune system deficiency ex vivo and activated lymphocytes can then be reimplanted in the subject.
>
> Immunostimulatory oligonucleotides can also be administered to a subject in conjunction with a vaccine, as an adjuvant, to boost a subject's immune system to effect better response from the vaccine. Preferably the unmethylated CpG dinucleotide is administered slightly before or at the same time as the vaccine.
>
> Preceding chemotherapy with an immunostimulatory oligonucleotide should prove useful for increasing the responsiveness of the malignant cells to subsequent chemotherapy. CpG ODN also increased natural killer cell activity in both human and murine cells. Induction of NK activity may likewise be beneficial in cancer immunotherapy.

In the section of the specification reproduced above, at least three therapeutic uses of immunostimulatory CpG oligonucleotides are provided: 1) Administration of an immunostimulatory CpG oligonucleotide to a subject with an immune system deficiency (in vivo and ex vivo); 2) Use of an immunostimulatory CpG oligonucleotide as a vaccine adjuvant; and 3) Use of an immunostimulatory CpG oligonucleotide in conjunction with a chemotherapy. The first two are of relevance here. Throughout the Office Action, the Examiner appears to have focused on the embodiment drawn to the second therapeutic use, namely, use of an immunostimulatory CpG oligonucleotide as an adjuvant, and improperly disregarded the embodiment drawn to the first use, which is to administer to a subject an immunostimulatory CpG oligonucleotide so as to boost the subject's immune system.

Ample evidence is provided in the specification, going back to the priority document, to demonstrate the immunostimulatory oligonucleotides of the instant invention can boost a subject's immune system. The data in the application establishes that the unmethylated CpG is responsbile for the immune stimulation. The data are consistent with the broad teachings of the invention that unmethylated CpG oligonucleotides stimulate an immune response, including B cell activation, NK cell stimulation, IgM production and IL-6 and IL-12 induction. Collectively, one of ordinary skill in the art would reasonably conclude that an unmethylated CpG oigonucleotide can elicit immunostimulatory effects, and the immunostimulatory activity is not limited to its use as an adjuvant.

Applicant wishes to bring to the Examiner's attention the following post-filing references that support Applicant's teachings presented above.

Martinson et al. (Immunology, 120:526-35) provide further evidence that ODN with unmethylated CpG stimulate Toll-like receptor 9 (TLR9) and activate innate and adaptive immunity. The authors studied the impact of class A, B and C CpG oligonucleotides on the activation of innate immune cells of HIV-infected individuals and found that exposure of HIV-1-positive PBMC to all classes of CpG-ODNs led to activation and maturation of plasmacytoid dendritic cells at levels similar to HIV-1-negative cells. The authors further note that while HIV-1-infected individuals have fewer innate effector cells that are chronically activated, these cells can be further activated by CpG-ODNs, supporting that synthetic CpG-ODNs are useful for enhancing the immune system in HIV-1-infected individuals. A copy of Martinson et al. is submitted herewith for the Examiner's reference.

Again, this is not to say that the unmethylated immunostimulatory oligonucleotides of the instant invention are not useful as an adjuvant. In fact, as noted by the Examiner, data indicate that they are.

Cooper et al. (Clin. Infect. Disease, 46:1310-14) provide data that a CpG oligonucleotide that is used as an adjuvant in conjunction with Hepatitis B virus vaccination in HIV-infected adults achieves long-term seroprotection, indicating that the unmethylated immunostimulatory oligonucleotides recited in the claims are also useful as a vaccine adjuvant for subjects that are

generally hypo-responsive to vaccines. A copy of Cooper et al. is submitted herewith for the Examiner's reference.

The teachings of these recent references confirm the teaching of the instant specification that an unmethylated CpG nucleic acid is useful in boosting a subject's immune system, where the subject has an immune system deficiency associated with human immunodeficiency virus (HIV) infection. Based on the foregoing, Applicant asserts that the instant claims are enabled.

Accordingly, it is respectfully requested that the Examiner withdraw the rejection under § 112, first paragraph.

Double Patenting Rejection

Claims 1, 2, 87 and 88 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 37-43, 46-52,56-61 and 91-101 of copending Application No. 11/296,644. Claims 1, 2, and 88 stand provisionally rejected as allegedly unpatentable over claims 42-68 of copending Application No. 10/382,822. Claims 1 and 2 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 37-56 of copending Application No. 10/788,191.

Applicant notes that these rejections are provisional obviousness-type double patenting rejections because the allegedly conflicting claims have not yet been patented. Applicant will address these rejection if and when one or more of the allegedly conflicting claims become allowable.

The Examiner further provisionally rejected claims 1 and 2 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 19-33 of

copending Application No. 10/987,146. Claims 1, 2, and 88 stand provisionally rejected as allegedly unpatentable over claims 37-65 of copending Application No. 11/067,516.

Applicant wishes to bring to the Examiner's attention that co-pending Applications 10/987,146 and 11/067,516 are now abandoned. As such, the rejection under the judicially created doctrine of obviousness-type double patenting based on the above-referenced co-pending Applications 10/987,146 and 11/067,516 is rendered moot. Accordingly, Applicant respectfully requests withdrawal of the double patenting rejections.

Based on the forgoing, Applicant believes that the claims as amended herein are now in an allowable condition. A favorable response is earnestly solicited.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1039.70084US00

Dated: June 9, 2008

Respectfully submitted,

By /Patrick R. H. Waller/
Patrick R.H. Waller
Registration No.: 41,418
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000